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David Hands

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EXAMINER

LOEWE, SUN JAE Y

ART UNIT

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1626

MAIL DATE

DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

DETAILED ACTION

1. Claims 28 and 30-46 are pending in the instant application.

Response to Arguments

2. The arguments filed on April 6, 2009 have been fully considered, however, they are not persuasive in overcoming the 35 USC 103 rejection. This ground of rejection is maintained and made FINAL. Below are responses to Applicant's remarks.

There would have been no motivation in U.S. Patent No. 5,719,147 to have used the hydrochloride salt of the compound 2-(R)-(1-(R)-(3,5-bis(trifluoromethyl)phenyl)ethoxy)-3-(S)-(4-fluoro)phenylmorpholine. In fact, Example 75 (with reference to Example 70) of U.S. Patent No. 5,719,147 teaches away from the present invention by indicating that the free base of the compound 2-(R)-(1-(R)-(3,5-bis(trifluoromethyl)phenyl)ethoxy)-3-(S)-(4-fluoro)phenylmorpholine should be employed.

Embodiments taught in the reference use hydrochloride salt as starting material. Eg. see example 101.

There would have been no motivation in U.S. Patent No. 5,719,147 to have conducted the cyclization process at a temperature of about 140-150°C. Example 75 (by reference to Example 70) indicates that 2-(R)-(1-(R)-(3,5-bis(trifluoromethyl)phenyl)ethoxy)-3-(S)-(4-fluoro)-phenyl-4-(3-(5-oxo-1,2,4-triazolo)methyl)morpholine was prepared by heating 2-(R)-(1-(R)-(3,5-bis(trifluoromethyl)phenyl)-ethoxy)-3-(S)-(4-fluoro)phenyl-4-(2-N-methylcarboxy-acetamidrazono)morpholine in 15 ml a mixture of xylenes at reflux for 2 hours. The CRC Handbook of Chemistry and Physics indicates that the boiling point of o-xylene is 144°C, the boiling point of m-xylene is 139°C, and the boiling point of p-xylene is 138°C. There is no indication that the process conditions in Example 75 of heating at reflux in a mixture of xylenes would have actually corresponded to a temperature of 140-150°C and, alternatively, there would have been no direction regarding how the temperature should have been changed.

Heating at reflux in xylenes (ie. mixture of xylenes boiling at 138, 139 and 144) corresponds to the claimed temperature of 140-150 degrees Celsius.

There would have been no motivation in U.S. Patent No. 5,719,147 to use toluene, rather than xylenes. U.S. Patent No. 5,719,147 does not disclose or suggest the use of toluene in any reactions comparable to the claimed process. In fact, Example 75 and similar disclosure in U.S. Patent No. 5,719,147 teaches away from the present invention by suggesting that the xylenes should be employed as the reaction solvent for the alkylation reaction.

Prior art provides for the use of toluene in different embodiments, eg. see example 101.

There would have been no motivation in U.S. Patent No. 5,719,147 to use an inorganic base, rather than the organic base such as N,N-diisopropylethylamine. In fact, U.S. Patent No. 5,719,147 teaches away from the present invention by suggesting that an organic base such as N,N-diisopropylethylamine should have been employed.

Embodiments within the reference provide for the use of inorganic base, see example 17.

There would have been no motivation in U.S. Patent No. 5,719,147 to use a specific solvent which is selected from dimethylformamide, dimethylsulfoxide, N-methylpyrrolidone, acetonitrile, N,N-dimethylacetamide and hexamethylphosphoramide, rather than acetonitrile. In fact, U.S. Patent No. 5,719,147 teaches away from the present invention by suggesting that the acetonitrile would have been required.

Embodiments within the reference provide for the use of specific solvents such as DMF – see example 17.

Even if one of ordinary skill in the art had been motivated to alter the process disclosed in U.S. Patent No. 5,719,147, there would have been no direction in U.S. Patent No. 5,719,147 regarding which specific reagents, solvents, temperature, additional steps and/or other conditions should have been employed in the process.

By routine experimentation, one of ordinary skill can practice various processes (including instant invention) wherein the experimental conditions are altered, with a reasonable expectation of success. The process claimed is taught by the prior art. The modification of the conditions of the process is within the level of ordinary skill – with suggestion based on the various embodiments disclosed (eg. see embodiments noted above and in the office action dated November 6, 2009).

also minimizes the use of toxic solvents. Surprisingly, the present invention also gives the desired compound in 85% yield (page 8, lines 8-9), which is unexpectedly higher than the yield disclosed for the procedure in U.S. Patent No. 5,719,147 (79% yield) (Example 75, column 104).

The change in yield does not appear to be unexpected. Applicant is requested to provide a showing/declaration stating the reasons/explaining why the noted difference in yield is unexpected.

Conclusion

3. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUN JAE Y. LOEWE whose telephone number is (571)272-9074. The examiner can normally be reached on M-F 7:30-5:00 Est.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR

Art Unit: 1626

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/Golam M. M. Shameem/
Primary Examiner, Art Unit 1626

/Sun Jae Y. Loewe/
6-17-2009